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Analysis of Bilateral Neck Metastasis of Tongue Cancer

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Abstract: To estimate the prognosis of bilateral cervical metastases from tongue carcinoma, we studied twelve patients (24-72 years old) who underwent neck dissections at our hospital to judge whether we should have performed radical treatment or not for those patients of tongue carcinoma who had bilateral metastatic nodes.

The five-year survival rate of bilateral neck metastasis patients was 58% (the Kaplan-Meier method). On the other hand, the five-year survival rate of patients with only unilateral neck metastases of squamous cell carcinoma of the tongue was 56%. Thus, there was no statistical significant difference in survival rate.

We conclude that even if a patient has metastatic lymph nodes on both sides of the neck, radical therapy should be done.

Key words: Tongue cancer, Bilateral metastasis, Contralateral metastasis, Survival rate, Neck dissection

Introduction

Squamous cell carcinoma of the tongue with bilateral lymph node involvement, namely N2c, is classified as advanced carcinoma, clinical stage IV by UICC, regardless of T stage. Such patients have a poor prognosis. One report found that patients with bilateral cervical metastases had an expected survival that was 25% that of patients with no metastatic nodes[1]. While the presence of bilateral metastasis might decrease a patient's survival rate, radical surgery may worsen their QOL[2,3].

We have retrospectively reviewed cases involving patients who underwent lymph node dissection at our hospital to determine whether radical therapy was indicated for patients with tongue cancer who had bilateral metastatic lymph nodes.

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Materials and methods

A retrospective analysis was done of 12 patients undergoing bilateral neck dissection from a consecutive series of 81 patients with oral tongue squamous cell carcinoma who underwent surgical resection of a primary tumor in Tokyo Medical and Dental University Hospital from 1988 to 2002. None of the patients showed clinical signs of recurrent disease prior to undergoing neck dissection. Of the 81 patients, 12 underwent bilateral neck dissection and 69 underwent unilateral neck dissection. All demonstrated nodal metastasis pathologically.

Of the 12 patients included in the present study, 7 were men (58%) and 5 were women (42%). The age range was from 24 to 75 years (mean age, 57.6).

T stages identified were two cases of T1, eight of T2, and two of T4. Clinical N stages identified were six cases of N0, two of N2b, and four of N2c.

Tumor sites were the anterior one third of the tongue border in one case, the middle one third of the tongue border in five cases, the posterior one third of the tongue border in three cases, the middle and posterior

Table 1 Cases of tongue cancer examined

Patient	Age, Sex	Site	TN Classification	Histological Grade	Primary treatment	Neck dissection		Duration (days) Ipsilateral → Contra lateral	Outcome
						Ipsilateral	Contralateral		
1	44, F	Middle-Posterior	T4N2b	I	Ope	Primary + RND	Delayed RND	145	Dc
2	75, M	Posterior	T1N2b	I	Ope	Primary + RND	Delayed RND	246	Dc
3	67, M	Middle	T2N0	I	Rad	Delayed RND	Delayed RND	77	Dc
4	24, F	Posterior	T2N2c	Ⅱ～Ⅲ	Rad + Ope	Primary + RND	Primary + MRND	0	Dc
5	73, M	Anterior	T2N0	I	Ope	Primary + SOHND	Delayed RND	49	Dc
6	70, F	Posterior	T2N0	I	Ope	Delayed RND	Delayed RND	317	A0
7	41, M	Dorsum	T4N2c	I～Ⅱ	C + Ope	Primary + RND	Primary + MRND	0	A0
8	59, F	Middle	rT2N2c	I	Ope	Primary + RND	Primary + MRND	0	A0
9	53, M	Middle	T2N0	I～Ⅱ	Rad	Delayed RND	Delayed RND	40	A0
10	59, F	Middle	T2N2c	I～Ⅱ	Ope	Primary + RND	Primary + MRND	0	A0
11	54, M	Middle	T1N0	Ⅱ～Ⅲ	Ope	Delayed RND	Delayed MRND	0	A0
12	72, M	Inferior surface	T2N0	Ⅱ～Ⅲ	Ope	Primary + MRND	Delayed RND	98	A0

Rad: Radiation C: Chemotherapy RND: Radical neck dissection
MRND: Modiffied neck dissection SOHND: Supraomohyoid neck dissection

tongue border in one case, the tongue dorsum in one case, and the inferior surface of the tongue in one case. Analysis of grade of histologic differentiation identified six cases of well-differentiated squamous cell carcinoma (grade Ⅰ), three of moderately differentiated (grade Ⅱ), and three of undifferentiated (grade Ⅲ) (Table 1).

Of the 12 patients undergoing bilateral neck dissection, five were continuous dissections and seven were discontinuous. The types of ipsilateral neck dissection used were radical classic in four cases and modified radical with preservation of the internal jugular vein in one case. All operations consisted of therapeutic neck dissections aside from one case of SOHND (Case No. 5).

Probability of survival at the five-year follow-up was calculated using the Kaplan-Meier method, and differences between curves were evaluated by the log-rank test. Statistical analysis was done using the SPSS program (SPSS Inc., Chicago, III, version 11).

Results

The duration of ipsilateral neck dissection to contralateral neck dissection was variable, lasting from 40 days to 317 days, but close to 83% of all patients had metastasized within 180 days to the regional lymph nodes (Table 1).

Table 2 shows the relationship between level of metastatic lymph nodes and size in specimens taken from twelve neck dissections including ipsilateral and contralateral. Fewer contralateral metastatic lymph nodes were found in levels I to III than ipsilateral. The number of lymph nodes at ipsilateral levels I, II, III and IV was 10, 14, 12 and one, respectively, whereas the respective values for contralateral were nine, nine, four, and five. Almost all metastatic lymph nodes in the ipsilateral and contralateral neck were at 'sentinel lymph nodes', the first lymphatic drainage, namely level I to level III, 97% (36/37) and 81% (22/27), respectively.

There were four cases with more than three contralateral metastatic nodes, and all four patients died (Table 2). There is a statistically significant difference in the maximum size of contralateral metastatic nodes between groups Dc and A0 (P = 0.048, Mann-Whitney's U test), but there is no statistically significant difference in the ipsilateral metastatic nodes.

The patient outcomes are presented in Table 1. Table 2 shows the relationship between contralateral metastatic lymph node level (the most distal portions) and survival rate. The survival rate was lower in levels III and IV (33.3%) than in levels I and II (85.7%).

Among five cases resulting in death, the cause of death was neck uncontrolled in one case, primary uncontrolled in one case, both primary and neck uncontrolled in two cases, and distant metastasis in one case.

The five-year survival rate among cases with bilateral neck metastasis was 58% according to the Kaplan-Meier method. In contrast, the Kaplan-Meier five-year surviv-

Table 2 Distribution of cases according to the level of metastatic lymph nodes and their number and size in the twelve cases which underwent to a neck dissection

Level / Patients	Ipsilateral				Contralateral			
	I	II	III	IV	I	II	III	IV
1	2(32)		4				1(25)	2
2		3(18)	2		2	1	2(23)	
3	2(26)	1			2(42)	1	1	
4		1(50)	1			4(35)		1
5	1(6)				1(15)			
6	1(26)				1(14)			1
7		3(30)	2			2(19)		
8		2(16)	1			1(16)		
9	1	2(26)	2	1	1(15)			
10	1(15)				1(16)			
11	1(11)	1			1(14)			
12	1(13)	1						1(23)

( ) : Maximum size (mm) of nodes in unilateral neck specimen

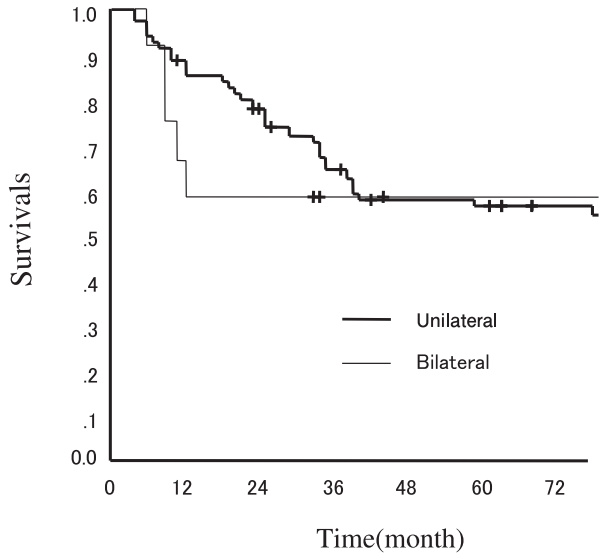

Fig. 1 Survival curves after surgery according to bilateral metastases and unilateral metastasis.

al rate among 69 cases of unilateral neck metastases of squamous cell carcinoma of the tongue was 56%; there was no statistically significant difference in survival between the two groups (P = 0.81) (Fig. 1).

Discussion

All of the present cases showed contralateral neck metastasis within one year after ipsilateral neck dissection. Thus, for patients undergoing unilateral neck dissection, an examination of contralateral lymph nodes should be performed within at least one year.

A comparison of neck node levels between the ipsilateral and contralateral metastatic lymph nodes reveals that the routes of metastasis to the contralateral neck were very similar to the ipsilateral route, given that 80% of lymphatic metastases for both contralateral and ipsilateral metastases developed in level I to level III, which are considered to be the first lymphatic drainage for tongue carcinoma. These findings are compatible with the hypothesis that lymphatic drainage in the tongue comprises a bilateral lymphatic network. It is thus very likely that some of the present cases of bilateral metastases developed metastasis on both sides at the same time or there was a significant delay following operation on the primary site. This suggests that bilateral metastases developed via the same mechanism as unilateral metastases.

We concluded that contralateral neck metastasis was likely the result of an occult metastasis (subclinical metastasis) of the cervical lymph nodes[4]. Magrin et al.[2] reported that bilateral neck dissection was associated with high morbidity and is contraindicated as an elective procedure.

A few reports in the literature have examined the mechanism underlying the risk of bilateral metastases with respect to lymphatic drainage. Werner et al.[5] examined 850 specimens of the upper aerodigestive tract (UADT), including 362 specimens collected at autopsy and 488 collected intraoperatively, to survey the architecture and drainage pattern of the lymphatic system of the UADT. They found bilateral drainage pathways in nearly all areas of the UADT, including the tongue.

Mukherji et al.[6] also reported that cross-drainage in the oral tongue is common.

Kowalski et al.[7] demonstrated by multivariate logistic regression analysis that the most important predictors of contralateral metastasis are clinical stage, a tumor crossing midline, and floor of the mouth involvement.

We concluded that there is a greater degree of ipsilateral lymphatic drainage than contralateral drainage, since ipsilateral metastatic lymph nodes outnumbered contralateral nodes in this study.

The literature contains many descriptions of poor prognosis among patients presenting with bilateral cervical metastases[8–11]. Kowalski et al.[12] stated that the finding of contralateral metastases in one single lymph node and the presence of metastases restricted to levels I and II did not lead to a poor prognosis. But they also stated that none of the cases with contralateral lymph node involvement at levels III or IV survived until the five-year follow-up. Five cases were simultaneous neck metastasis. Simultaneous bilateral neck dissection was done in four cases, and all patients survived. Cases were analyzed according to the size of the contralateral lymph node and level of involvement, and two factors contributing to the patients' survival were identified: a relatively small node and the presence of metastases restricted to levels I and II.

Five of six patients who had neck metastasis in the level III or IV regions underwent neck dissection for late neck metastasis after initial operation, while only one patient underwent simultaneous neck dissection. We considered that the contralateral nodes metastasis originally existed at the initial neck dissection because the primary tumor had been controlled. The time lag from initial neck dissection to late neck dissection might have caused metastases at more distal lymph nodes. In addition the maximum size of contralateral metastatic lymph nodes was larger in the Dc group in which a significant difference in size was present.

Therefore, the immediate detection of contralateral neck metastasis and treatment of neck disease should be considered for patients with bilateral neck metastasis to improve their outcome.

Umeda et al.[13] reported that bilateral cervical metastases from oral carcinomas are not always associated with a poor prognosis.

No difference in survival rate was found between unilateral and bilateral metastasis in the present study. We concluded that bilateral metastasis on its own is not an indicator of poor prognosis, whereas the site of cervical metastasis, a positive node in or out of the sentinel node area, the first echelon of lymphatic drainage, and size or number of metastatic lymph nodes were prognostic factors, as they are in cases of unilateral cervical metastasis.

Conclusion

One limitation of the present study is that the number of cases was too small to draw a conclusion, but we recognized the following tendency.

Not all of the tongue carcinomas with metastatic lymph nodes showed a poor prognosis. Therefore, we concluded that even if a patient has metastatic lymph nodes on both sides of the neck, radical therapy should be performed.

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